

## Brg1 governs distinct pathways to direct multiple aspects of mammalian neural crest cell development.

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### Public Summary:

This article addresses how chromatin regulators function in the neural crest stem cells to regulate cardiovascular development in the embryos.

### Scientific Abstract:

Development of the cerebral vessels, pharyngeal arch arteries (PAAs), and cardiac outflow tract (OFT) requires multipotent neural crest cells (NCCs) that migrate from the neural tube to target tissue destinations. Little is known about how mammalian NCC development is orchestrated by gene programming at the chromatin level, however. Here we show that Brahma-related gene 1 (Brg1), an ATPase subunit of the Brg1/Brahma-associated factor (BAF) chromatin-remodeling complex, is required in NCCs to direct cardiovascular development. Mouse embryos lacking Brg1 in NCCs display immature cerebral vessels, aberrant PAA patterning, and shortened OFT. Brg1 suppresses an apoptosis factor, Apoptosis signal-regulating kinase 1 (Ask1), and a cell cycle inhibitor, p21(cip1), to inhibit apoptosis and promote proliferation of NCCs, thereby maintaining a multipotent cell reservoir at the neural crest. Brg1 also supports Myosin heavy chain 11 (Myh11) expression to allow NCCs to develop into mature vascular smooth muscle cells of cerebral vessels. Within NCCs, Brg1 partners with chromatin remodeler Chromodomain-helicase-DNA-binding protein 7 (Chd7) on the PlexinA2 promoter to activate PlexinA2, which encodes a receptor for semaphorin to guide NCCs into the OFT. Our findings reveal an important role for Brg1 and its downstream pathways in the survival, differentiation, and migration of the multipotent NCCs critical for mammalian cardiovascular development.

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